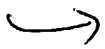
```
    FILE 'CAPLUS, MEDLINE' ENTERED AT 14:34:15 ON 04 MAY 2004
L1             9 S (OSTEOARTHRIT? OR RHEUMATOID ARTHRITIS) (50A) (BLOOD (10A) (V

=> d que
L1             9 SEA (OSTEOARTHRIT? OR RHEUMATOID ARTHRITIS) (50A) (BLOOD (10A)
                 (VISCOSITY OR VISCOUS))


=>
```



See next page also.

inventor name search.

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FILE 'CAPLUS, WPIDS, MEDLINE' ENTERED AT 15:34:18 ON 04 MAY 2004
            E MANION CARL/IN,AU
            E MANION C/IN,AU
L1          55 S E16-E22
L2          28 S L1 AND (BLOOD OR ANTITHROMB? OR VISCOSITY)
L3          20 DUP REM L2 (8 DUPLICATES REMOVED)

=>
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Next page has

Aspartame + other Diseases that may be assoc'd w/ ↑ Blood Viscosity

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     FILE 'REGISTRY' ENTERED AT 15:40:56 ON 04 MAY 2004
L1             1 S ASPARTAME/CN
                 SEL CHEM L1
L2               QUE E1-E7 OR E9-E21

     FILE 'CAPLUS, WPIDS, MEDLINE, PHIC, PHIN' ENTERED AT 15:42:36 ON 04 MAY
     2004
L3          5858 S L2
L4             1 S L3 AND MULTIPLE MYELOM?
L5             4 S L3 AND (MACROGLOBULINEM? OR PLASMA CELL DYSCRAS? OR DYSPROTEI
L6             4 DUP REM L5 (0 DUPLICATES REMOVED)

=> d que
L2               QUE  (".ALPHA.-L-ASPARTYL-L-PHENYLALANINE METHYL ESTER"/B
                 I OR .ALPHA.-SWEET/BI OR ASPARTAME/BI OR "ASPARTYLPHENYLA
                 LANINE METHYL ESTER"/BI OR CANDEREL/BI OR "DIPEPTIDE SWEE
                 TENER"/BI OR "E 951"/BI) OR ("L-.ALPHA.-ASPARTYL-L-PHENYL
                 ALANINE METHYL ESTER"/BI OR "L-ASPARTYL-L-PHENYLALANINE M
                 ETHYL ESTER"/BI OR "L-ASPARTYL-L-PHENYLALANYL METHYL ESTE
                 R"/BI OR "L-ASPARTYL-L-3-PHENYLALANINE METHYL ESTER"/BI O
                 R "METHYL ASPARTYLPHENYLALANATE"/BI OR NUTRASWEET/BI OR "
                 PAL SWEET"/BI OR "PALSWEET DIET"/BI OR "SWEET DIPEPTIDE"/
                 BI OR 172964-81-7/BI OR 22839-47-0/BI OR 53906-69-7/BI OR
                  7421-84-3/BI)
L3          5858 SEA L2
L5             4 SEA L3 AND (MACROGLOBULINEM? OR PLASMA CELL DYSCRAS? OR
                 DYSPROTEINEM? OR (BLOOD (5A) VISCO?))
L6             4 DUP REM L5 (0 DUPLICATES REMOVED)


=>
```

L4 1 L3 AND MULTIPLE MYELOM?

=> d

L4 ANSWER 1 OF 1 MEDLINE on STN
AN 2000424397 MEDLINE
DN PubMed ID: 10931557
TI Binding of nascent collagen by amyloidogenic light chains and amyloid fibrillogenesis in monolayers of human fibrocytes.
AU Harris D L; King E; Ramsland P A; Edmundson A B
CS Department of Biology, University of Utah, Salt Lake City, UT 84112, USA.
NC CA72803 (NCI)
SO Journal of molecular recognition : JMR, (2000 Jul-Aug) 13 (4) 198-212.
Journal code: 9004580. ISSN: 0952-3499.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000914

=> s l3 and (macroglobulinem? or plasma cell dyscras? or dysproteinem? or (blood (5a) visco?))
L5 4 L3 AND (MACROGLOBULINEM? OR PLASMA CELL DYSCRAS? OR DYSPROTEINEM ? OR (BLOOD (5A) VISCO?))

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 4 DUP REM L5 (0 DUPLICATES REMOVED)

=> d 1-4 bib ab kwic

L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:247195 CAPLUS
DN 134:261255
TI N-L-.alpha.-aspartyl-L-phenylalanine 1-Me ester as **blood viscosity**-modulating substance, and use thereof
IN Manion, Carl V.
PA Oklahoma Medical Research Foundation, USA
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001022983	A2	20010405	WO 2000-US25874	20000921
	WO 2001022983	A3	20010816		
	W: AU, CA, MX, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1218024	A2	20020703	EP 2000-963682	20000921
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	US 1999-156119P	P	19990925		
	WO 2000-US25874	W	20000921		

AB N-L-.alpha.-aspartyl-L-phenylalanine 1-Me ester (APM) (or other alkyl ester) lowers whole **blood viscosity** in patients, including those suffering from sickle cell disease and **plasma**

cell dyscrasias. Upon in vivo APM treatment, patients experienced a significant lowering of whole **blood viscosity.** In vitro addn. of APM to patients samples having elevated whole **blood viscosity** resulted in reduced **viscosity** over time. These in vitro and in vivo results identify APM as a therapeutic agent for mol. diseases which lead to elevated whole **blood viscosity.** A method by which APM treatment can be monitored is also disclosed.

TI N-L-.alpha.-aspartyl-L-phenylalanine 1-Me ester as **blood viscosity**-modulating substance, and use thereof

AB N-L-.alpha.-aspartyl-L-phenylalanine 1-Me ester (APM) (or other alkyl ester) lowers whole **blood viscosity** in patients, including those suffering from sickle cell disease and **plasma cell dyscrasias.** Upon in vivo APM treatment, patients experienced a significant lowering of whole **blood viscosity.** In vitro addn. of APM to patients samples having elevated whole **blood viscosity** resulted in reduced **viscosity** over time. These in vitro and in vivo results identify APM as a therapeutic agent for mol. diseases which lead to elevated whole **blood viscosity.** A method by which APM treatment can be monitored is also disclosed.

ST aspartyl phenylalanine methyl ester **blood viscosity**

IT Blood
Cardiovascular agents
Sickle cell anemia
Viscosity
(aspartyl phenylalanine Me ester as **blood viscosity** -modulating substance)

IT Drug delivery systems
(unit doses; aspartyl phenylalanine Me ester as **blood viscosity**-modulating substance)

IT 13433-09-5D, alkyl esters with phenylalanyl carboxyl moiety
22839-47-0, Aspartame
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aspartyl phenylalanine Me ester as **blood viscosity** -modulating substance)

L6 ANSWER 2 OF 4 MEDLINE on STN
AN 2001277727 MEDLINE
DN PubMed ID: 11372003
TI **Aspartame** effect in sickle cell anemia.
AU Manion C V; Howard J; Ogle B; Parkhurst J; Edmundson A
CS Department of Clinical Pharmacology, Oklahoma Medical Research Foundation, Oklahoma City, OK 73112, USA.
NC CA 72803 (NCI)
SO Clinical pharmacology and therapeutics, (2001 May) 69 (5) 346-55. Journal code: 0372741. ISSN: 0009-9236.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200106
ED Entered STN: 20010618
Last Updated on STN: 20010618
Entered Medline: 20010614

AB OBJECTIVE: To examine the in vitro and in vivo attributes of **aspartame** and to determine its efficacy for treating sickle cell anemia. RATIONALE: **Aspartame** (**l-aspartyl-**

l-phenylalanine methyl ester) binds with 2 human Bence Jones proteins. The proteins (Mcg and Sea) showed phenylalanine penetrating into hydrophobic binding sites. This **aspartame** property suggested a potential to interfere with sickle hemoglobin fibril formation. METHODS: For the in vitro studies, blood from 20 subjects monitored for sickle cell anemia was collected in heparinized tubes. Specimens were divided in thirds and **aspartame** was added to 2 tubes to yield a 1 mg/mL or 2 mg/mL concentration. Sickled cells that were present after a drop from each aliquot was added to a fresh 2% metabisulfite solution were counted 3 times. For the in vivo studies, 23 subjects from the Sickle Cell Clinic (University of Oklahoma Health Sciences Center, Oklahoma City, Okla) consented to participate in a randomized single-dose administration of 1.5, 3.0, or 6 mg/kg **aspartame**. Heparinized blood was obtained at 0, 30, 60, 120, 240, 480, and 1440 minutes after **aspartame** administration. Specimens were counted in a blinded manner by means of the technique used for the in vitro method, but a photomicrograph of 1 field from each triplicate count was made. The pictures were marked and were computer counted. RESULTS: For the in vitro studies, sickled cells decreased from 28% to < 14% when 1 mg/mL **aspartame** was added and decreased further with 2 mg/mL. For the in vivo studies, a decreased number of sickled cells in homozygous blood (HbSS) were observed after oral administration of **aspartame** . Sickling was inhibited by 6 mg/kg **aspartame** for at least 6 hours in 15 subjects with HbSS anemia. CONCLUSIONS: Further evaluations of the efficacy of **aspartame** for sickle crisis and crisis prevention appears to be warranted.

TI **Aspartame** effect in sickle cell anemia.

AB OBJECTIVE: To examine the in vitro and in vivo attributes of **aspartame** and to determine its efficacy for treating sickle cell anemia. RATIONALE: **Aspartame** (**l-aspartyl-l-phenylalanine methyl ester**) binds with 2 human Bence Jones proteins. The proteins (Mcg and Sea) showed phenylalanine penetrating into hydrophobic binding sites. This **aspartame** property suggested a potential to interfere with sickle hemoglobin fibril formation. METHODS: For the in vitro studies, blood from 20 subjects monitored for sickle cell anemia was collected in heparinized tubes. Specimens were divided in thirds and **aspartame** was added to 2 tubes to yield a 1 mg/mL or 2 mg/mL concentration. Sickled cells that were present after. . . Health Sciences Center, Oklahoma City, Okla) consented to participate in a randomized single-dose administration of 1.5, 3.0, or 6 mg/kg **aspartame**. Heparinized blood was obtained at 0, 30, 60, 120, 240, 480, and 1440 minutes after **aspartame** administration. Specimens were counted in a blinded manner by means of the technique used for the in vitro method, but. . . were computer counted. RESULTS: For the in vitro studies, sickled cells decreased from 28% to < 14% when 1 mg/mL **aspartame** was added and decreased further with 2 mg/mL. For the in vivo studies, a decreased number of sickled cells in homozygous blood (HbSS) were observed after oral administration of **aspartame**. Sickling was inhibited by 6 mg/kg **aspartame** for at least 6 hours in 15 subjects with HbSS anemia. CONCLUSIONS: Further evaluations of the efficacy of **aspartame** for sickle crisis and crisis prevention appears to be warranted.

CT . . . Gov't; Support, U.S. Gov't, P.H.S.
Administration, Oral
Adolescent
Adult
*Anemia, Sickle Cell: DT, drug therapy
Anemia, Sickle Cell: GE, genetics
***Aspartame: TU, therapeutic use**
*Blood: DE, drug effects
Blood Viscosity: DE, drug effects

Child
Child, Preschool
Genotype
Middle Aged

RN **22839-47-0 (Aspartame)**

L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:227518 CAPLUS
DN 132:260685
TI Inhibition of erythrocyte sickling by N-L-.alpha.-aspartyl-L-phenylalanine 1-methyl ester
IN Manion, Carl V.; Edmundson, Allen B.
PA Oklahoma Medical Research Foundation, USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000018418	A2	20000406	WO 1999-US22268	19990925
	WO 2000018418	A3	20000720		
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2345243	AA	20000406	CA 1999-2345243	19990925
	AU 9964008	A1	20000417	AU 1999-64008	19990925
	AU 769651	B2	20040129		
	EP 1115414	A2	20010718	EP 1999-951596	19990925
	EP 1115414	B1	20031217		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002525334	T2	20020813	JP 2000-571936	19990925
	AT 256474	E	20040115	AT 1999-951596	19990925
	US 6384076	B1	20020507	US 2001-787994	20010322
PRAI	US 1998-101876P	P	19980925		
	WO 1999-US22268	W	19990925		

OS MARPAT 132:260685
AB N-L-.alpha.-aspartyl-L-phenylalanine 1-Me ester (APM) exhibits antisickling properties. In vitro testing verified that APM significantly lowered the frequency of sickling of red blood cells from each of twelve pediatric aged patients being treated for sickle-cell anemia by exchange transfusion. Sickling was also inhibited in an "index" patient after oral administration of APM. These in vitro and in vivo results identify APM as a therapeutic agent for the family of sickle cell mol. diseases.
ST **aspartylphenylalanine methyl ester**
erythrocyte sickling inhibition; sickle cell disease
aspartylphenylalanine methyl ester; anemia
sickle cell **aspartylphenylalanine methyl ester**
IT **Blood** analysis
(**blood viscosity**; aspartylphenylalanine Me ester for inhibition of erythrocyte sickling)
IT **Viscosity**
(**blood**; aspartylphenylalanine Me ester for inhibition of erythrocyte sickling)
IT 13433-09-5D, esters **22839-47-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aspartylphenylalanine Me ester for inhibition of erythrocyte sickling)

L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:145092 CAPLUS
DN 126:143490
TI Producing method of high nutrient phosphatide oral liquid
IN Wang, Xizhao; Jin, Zhiguang; Tong, Qigen; Liu, Shuyi; Zhang, Fu; Zhang, Wentian; Liu, Wenxue
PA Zhaofu New Technology Development Co., Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1096686	A	19941228	CN 1993-107365	19930624
	CN 1039783	B	19980916		
PRAI	CN 1993-107365		19930624		

AB The process of making highly nutritious phosphatide oral liq. contg. soy bean phosphatide, vitamin E and unsatd. fatty acid is disclosed. It also contains cassia seed, Crataegus and essence. This oral liq. can lower **blood** lipid, **blood viscosity** and prevent arteriosclerosis.
AB The process of making highly nutritious phosphatide oral liq. contg. soy bean phosphatide, vitamin E and unsatd. fatty acid is disclosed. It also contains cassia seed, Crataegus and essence. This oral liq. can lower **blood** lipid, **blood viscosity** and prevent arteriosclerosis.
IT 50-81-7, Vitamin C, biological studies 4468-02-4, Zinc gluconate 15498-87-0, Selenious acid, sodium salt 16039-53-5, Zinc lactate **22839-47-0, Aspartame**
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(producing method of high nutrient phosphatide oral liq.)

=>